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**Stimulation of endogenous cardioblasts by exogenous cell therapy after myocardial infarction.**

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**Funding Grants:** Mechanism of heart regeneration by cardiosphere-derived cells

**Public Summary:**

Stimulation of endogenous cardioblasts by exogenous cells mediates therapeutic regeneration of injured myocardium.

**Scientific Abstract:**

Controversy surrounds the identity, origin, and physiologic role of endogenous cardiomyocyte progenitors in adult mammals. Using an inducible genetic labeling approach to identify small non-myocyte cells expressing cardiac markers, we find that activated endogenous cardioblasts are rarely evident in the normal adult mouse heart. However, myocardial infarction results in significant cardioblast activation at the site of injury. Genetically labeled isolated cardioblasts express cardiac transcription factors and sarcomeric proteins, exhibit spontaneous contractions, and form mature cardiomyocytes in vivo after injection into unlabeled recipient hearts. The activated cardioblasts do not arise from hematogenous seeding, cardiomyocyte dedifferentiation, or mere expansion of a preformed progenitor pool. Cell therapy with cardiosphere-derived cells amplifies innate cardioblast-mediated tissue regeneration, in part through the secretion of stromal cell-derived factor 1 by transplanted cells. Thus, stimulation of endogenous cardioblasts by exogenous cells mediates therapeutic regeneration of injured myocardium.

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